IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Application of: **Jon A. Wolff and Vladimir G. Budker**

Serial No.: **09/707,117**

Filed: **November 6, 2000**

Group Art Unit: **1632**

For: **Intravascular Delivery of Nucleic Acid**

RESPONSE TO COMMUNICATION

Assistant Commissioner for Patents
Washington, D.C. 20231

Dear Sir:

This is a response to the Communication dated September 26, 2002. Please attach this response as a supplement to the prior filed Amendment.

Support for the prior filed amendments found in the disclosure of the patent:

Teachings with respect to delivery of polynucleotide to skeletal muscle are found in the specification as follows:

Page 3, lines 4 and 5 of the specification states: "The parenchymal cell may consist of a muscle cell, such as a limb (leg or arm) muscle cell."

Page 10, lines 15-22 of the specification states: "In striated muscle, the parenchymal cells include myoblasts, satellite cells, myotubules, and myofibers. ... In one preferred embodiment striated muscle such as skeletal muscle or cardiac muscle is targeted by injecting the polynucleotide into the blood vessel supplying the tissue. In skeletal muscle an artery is the delivery vessel...."

Further support of the claimed invention providing delivery of polynucleotides to skeletal muscle is found in the examples, specifically: example 3 on page 25, example 7 on page 30, examples 8 and 9 on page 31 and example 10 on page 32.

Teachings with respect to applying pressure to the mammal's limb epidermis to impede blood flow are found in the specification as follows:

Page 5, lines 13-24 of the specification states: "The term cuff means a device for impeding blood flow through mammalian internal blood vessels. However, for purposes of the claims, cuff refers specifically to a device applied exterior to the mammal's skin and touches the skin in a non-invasive manner. ... The vessel walls are forced to constrict in an

area underneath the cuff in amount sufficient to impede blood from flowing at a normal rate. ... One example of a cuff is a sphygmomanometer which is normally used to measure pressure. In a preferred embodiment of this specification, the sphygmomanometer is used to apply pressure to mammalian skin, around a limb, for the purpose of increasing vessel permeability. Another example is a tourniquet.

In example 1 on page23, the use of a sphygmomanometer cuff surrounding the arm or leg proximal to the injection site to facilitate delivery of polynucleotides to muscle cells in primates is described. Similarly, the use of a tourniquet to facilitate delivery of polynucleotides to muscle cells in rats is described.

The data in examples 7 and 10 illustrate the increased delivery of polynucleotides to muscle tissue when blood flow occlusion is used during the process.

Teachings with respect to transient and continuous immunosuppression are found in the specification as follows:

Page 3, lines 26-33 of the specification states: "In a preferred embodiment it may be preferential to immunosuppress the host receiving the nucleic acid. Immunosuppression can be long term or for a short duration.... This can be accomplished by treatment with (combinations of) immunosuppressive drugs like cyclosporin A, ProGraf (FK506), corticosteroids, deoxyspergualin, and dexamethasone. Other methods include blocking of immune cell activation pathways ....

The use of immunosuppressive drugs to enhance or prolong expression of delivered polynucleotides is found in example 5 on page 28 and in examples 8 and 9 on page 31.

Teachings with respect to the delivery of polynucleotides resulting in expression at detectable levels are found in the specification in examples 3 and 5-10. In each of these examples, expression of delivered polynucleotide encoded genes is measured. These genes include the marker genes luciferase, β-galactosidase and SEAP as well as a therapeutic gene human factor IX.

Teachings with respect to maintaining limb function are found in the specification in examples 3 and 4. Example 3 states: "All seven monkeys tolerated the procedure well and had full function of their arms, hands, legs and feet following the procedure. In particular, this indicates lack of damage to the radial nerve.... Swelling in the target limbs, a putative correlate of successful gene transfer, was noted afterwards but completely subsided by the next day. It is noted in example 4 that the muscle tissue was well preserved and did not show any sign of pathology.

Respectfully submitted,

Mark K. Johnson Reg. No. 35,909
Mirus
505 South Rosa Road
Madison, WI 53719
608.238.4400

I hereby certify that this correspondence is being sent by facsimile transmission to the official fax number for Group 1632 at 703.308.4242 and is addressed to: Assistant Commissioner for Patents, Washington, DC 20231 on Friday, January 03, 2003.

Signature

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PTO/SB/21 (08-00)
Approved for use through 10/31/2002. OMB 0651-0031
U.S. Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE

TRANSMITTAL FORM

(to be used for all correspondence after initial filing)

Application Number	09/707,117
Filing Date	11/06/2000
First Named Inventor	Jon A. Wolff
Group Art Unit	1632
Examiner Name	Michael Wilson
Total Number of Pages In This Submission: 6	Attorney Docket Number: 18.02

ENCLOSURES *(check all that apply)*

- [x] Fee Transmittal Form
- [x] Fee Attached
- [x] Amendment / Reply
- [ ] After Final
- [ ] Affidavits/declaration(s)
- [x] Extension of Time Request
- [ ] Express Abandonment Request
- [ ] Information Disclosure Statement
- [ ] Certified Copy of Priority Document(s)
- [ ] Response to Missing Parts/ Incomplete Application
- [ ] Response to Missing Parts under 37 CFR 1.52 or 1.53
- [ ] Assignment Papers *(for an Application)*
- [ ] Drawing(s)
- [ ] Licensing-related Papers
- [ ] Petition
- [ ] Petition to Convert to a Provisional Application
- [ ] Power of Attorney, Revocation Change of Correspondence Address
- [ ] Terminal Disclaimer
- [ ] Request for Refund
- [ ] CD, Number of CD(s) _____
- [ ] After Allowance Communication to Group
- [ ] Appeal Communication to Board of Appeals and Interferences
- [ ] Appeal Communication to Group *(Appeal Notice, Brief, Reply Brief)*
- [ ] Proprietary Information
- [ ] Status Letter
- [ ] Other Enclosure(s) *(please identify below)*:

Remarks

SIGNATURE OF APPLICANT, ATTORNEY, OR AGENT

Firm or Individual name	Mark K. Johnson
Signature	
Date	01/03/2003

CERTIFICATE OF MAILING

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Typed or printed name	Mark K. Johnson		
Signature		Date	01/03/2003

PTO/SB/17 (10-01)
Approved for use through 10/31/2002. OMB 0651-0032
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

FEE TRANSMITTAL for FY 2003

Patent fees are subject to annual revision.

TOTAL AMOUNT OF PAYMENT ($) 460.00

Complete if Known	
Application Number	09/707,117
Filing Date	11/06/2000
First Named Inventor	Jon Wolff
Examiner Name	Michael Wilson
Group Art Unit	1633
Attorney Docket No.	Mirus.018.02

METHOD OF PAYMENT

1. ☐ The Commissioner is hereby authorized to charge indicated fees and credit any overpayments to:
   - Deposit Account Number
   - Deposit Account Name
   - ☐ Charge Any Additional Fee Required Under 37 CFR 1.16 and 1.17
   - ☐ Applicant claims small entity status. See 37 CFR 1.27
2. ☐ **Payment Enclosed:** ☐ Check ☑ Credit card ☐ Money Order ☐ Other

FEE CALCULATION

1. BASIC FILING FEE

Large Entity Fee Code	Large Entity Fee ($)	Small Entity Fee Code	Small Entity Fee ($)	Fee Description	Fee Paid
101	740	201	370	Utility filing fee	
106	330	206	165	Design filing fee	
107	510	207	255	Plant filing fee	
108	740	208	370	Reissue filing fee	
114	160	214	80	Provisional filing fee	

SUBTOTAL (1) ($)

2. EXTRA CLAIM FEES

	Extra Claims		Fee from below	Fee Paid
Total Claims		-20** =		x	=	
Independent Claims		- 3** =		x	=	
Multiple Dependent					=	

Large Entity Fee Code	Large Entity Fee ($)	Small Entity Fee Code	Small Entity Fee ($)	Fee Description
103	18	203	9	Claims in excess of 20
102	84	202	42	Independent claims in excess of 3
104	280	204	140	Multiple dependent claim, if not paid
109	84	209	42	** Reissue independent claims over original patent
110	18	210	9	** Reissue claims in excess of 20 and over original patent

SUBTOTAL (2) ($)

**or number previously paid, if greater; For Reissues, see above

FEE CALCULATION (continued)

3. ADDITIONAL FEES

Large Entity Fee Code	Large Entity Fee ($)	Small Entity Fee Code	Small Entity Fee ($)	Fee Description	Fee Paid
105	130	205	65	Surcharge - late filing fee or oath	
127	50	227	25	Surcharge - late provisional filing fee or cover sheet	
139	130	139	130	Non-English specification	
147	2,520	147	2,520	For filing a request for *ex parte* reexamination	
112	920*	112	920*	Requesting publication of SIR prior to Examiner action	
113	1,840*	113	1,840*	Requesting publication of SIR after Examiner action	
115	110	215	55	Extension for reply within first month	
116	400	216	200	Extension for reply within second month	
117	920	217	460	Extension for reply within third month	460.00
118	1,440	218	720	Extension for reply within fourth month	
128	1,960	228	980	Extension for reply within fifth month	
119	320	219	160	Notice of Appeal	
120	320	220	160	Filing a brief in support of an appeal	
121	280	221	140	Request for oral hearing	
138	1,510	138	1,510	Petition to institute a public use proceeding	
140	110	240	55	Petition to revive - unavoidable	
141	1,280	241	640	Petition to revive - unintentional	
142	1,280	242	640	Utility issue fee (or reissue)	
143	460	243	230	Design issue fee	
144	620	244	310	Plant issue fee	
122	130	122	130	Petitions to the Commissioner	
123	50	123	50	Processing fee under 37 CFR 1.17(q)	
126	180	126	180	Submission of Information Disclosure Stmt	
581	40	581	40	Recording each patent assignment per property (times number of properties)	
146	740	246	370	Filing a submission after final rejection (37 CFR § 1.129(a))	
149	740	249	370	For each additional invention to be examined (37 CFR § 1.129(b))	
179	740	279	370	Request for Continued Examination (RCE)	
169	900	169	900	Request for expedited examination of a design application	

Other fee (specify) _____

*Reduced by Basic Filing Fee Paid **SUBTOTAL (3)** ($) 460.00

SUBMITTED BY				Complete (if applicable)	
Name (Print/Type)	Mark K. Johnson	Registration No. (Attorney/Agent)	35,909	Telephone	262.821.5690
Signature				Date	01/03/2003

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